BioChem 330 - Course Outline

• **Metabolism and Bioenergetics (II)**
  – ENZYME CATALYSIS:
    • kinetic constants $k_{\text{cat}}$, $K_m$
    • Catalytic strategies, the serine proteases
  – CATABOLISM (*breakdown*)
    • Carbohydrates
      – Glycolysis
      – Tricarboxylic Acid Cycle
      – Electron Transport
      – Chemiosmosis and ATPase

• Fatty acids and amino acids
Fatty Acid Metabolism..... Proof of β oxidation

Odd-chain fatty acid

Even-chain fatty acid
Fatty Acid Metabolism..... Activated by CoA

Cytoplasmic enzyme: acyl CoA synthetase
Fatty Acid Metabolism....transported through mito via transferase – PART A

Carnitine (4-trimethylamino-3-hydroxybutyrate) ⇌ carnitine palmitoyl transferase

Acyl-carnitine
Fatty Acid Metabolism....transported through mito via transferase -PART B
Fatty Acid Metabolism — the mitochondrial details

1. Fatty acyl-CoA
   - FAD
   - acyl-CoA dehydrogenase (AD)
   - FADH₂
   - ETF (ubiquinone oxidoreductase)

2. trans-Δ²-Enoyl-CoA
   - H₂O
   - enoyl-CoA hydratase (EH)

3. 3-L-Hydroxyacyl-CoA
   - NAD⁺
   - 3-L-hydroxyacyl-CoA dehydrogenase (HAD)
   - NADH + H⁺

4. β-Ketoacyl-CoA
   - CoASH
   - β-ketoacyl-CoA thiolase (KT)

5. Reaction products:
   - CH₃(CH₂)n-C-SCoA
   - CH₃-C-SCoA

6. Electron transport chain
   - QH₂
   - Q
   - Mitochondrial electron transport chain
   - H₂O

7. 2ADP + 2Pi
   - 2ATP

8. O₂

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Fatty Acid Metabolism – FAM-4 KT details

CLAISEN ESTER CLEAVAGE
KT binds substrate at $C_\beta$ via a active site thiol

Tetrahedral Intermediate is formed with thioester

Bond cleavage between $C_\alpha$-$C_\beta$ occurs with collapse of this intermediate

Product 1, acetyl CoA liberated

Product 2, acyl CoA ready for another round

Figure 20-14
Fatty Acid Metabolism – dealing with unsaturation

Oleic acid
(9-cis-octadecenoic acid)

Linoleic acid
(9,12-cis-octadecadienoic acid)
Fatty Acid Metabolism – dealing with unsaturation

Figure 20-15

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Fatty Acid Metabolism – dealing with odd chain lengths

Three step process to convert the three C propionyl to four carbon succinyl CoA

1. Enzyme has biotin and resembles pyruvate decarboxylase.
2. Racemization from S to R stereoisomer
3. STRANGE C skeleton rearrangement that uses vitamin B12 (deficiency is known as pernicious anemia)
\[
\text{methylmalonyl-CoA mutase}
\]

\[
\begin{align*}
\text{CoAS} & \quad \text{C} & \quad \text{H} \\
\text{O} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{H} & \quad \text{C} & \quad \text{SCoA} \\
\end{align*}
\]

\[
\begin{align*}
\text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} \\
\end{align*}
\]

\[
\begin{align*}
\text{(R)-Methylmalonyl-CoA} & \quad \text{Carbon skeleton} & \quad \text{Succinyl-CoA} \\
\end{align*}
\]
Fate of acetyl CoA in liver is not TCA..... but KETONE BODIES

Acetoacetate

H₃C—C—CH₂—C O⁻

Acetone

H₃C—C—CH₃

D-β-Hydroxybutyrate

H₃C—C—CH₂—C O⁻
Three enzymic reactions transform acetyl CoA to beta keto acid

Liver releases acetoacetate and β-hydroxybutyrate to the blood to peripheral tissue for alternative fuels...

![Chemical reactions diagram]

Acetoacetate  
D-β-Hydroxybutyrate

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Figure 20-21
Fatty Acids are made in the cytoplasm in processes that are the reverse of beta oxidation.